(FILE 'HOME' ENTERED AT 10:59:49 ON 09 MAY 2005) FILE 'REGISTRY' ENTERED AT 11:13:41 ON 09 MAY 2005 1 S 72542-49-5 L1E OXYSTEROL/CN E OXYSTEROL L2193 S E3 FILE 'CAPLUS' ENTERED AT 11:18:14 ON 09 MAY 2005 1116 S OXYSTEROL L36 S L1 AND OXYSTEROL L4 L5 205 S (EPOXYCHOLESTEROL) OR OXIDOCHOLESTEROL 55 S L5(L) OXYSTEROL L6 L7 78 S L5(3A)(24 OR 25) L832 S OXYSTEROL#(L)L7 L9 14 S L8 NOT PY >=2000 FILE 'EPFULL, FRFULL, GBFULL, PATDPAFULL, PCTFULL, RDISCLOSURE, USPATFULL, USPAT2' ENTERED AT 11:40:26 ON 09 MAY 2005

E TULARIK/PA

472 S E3-E11 L10

L11 19 S L10 AND (OXYSTEROL OR OXIDOCHOLESTEROL OR EPOXYCHOLESTEROL O

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=> s e3-e11
```

L10

472 (TULARIK/PA OR "TULARIK INC"/PA OR "TULARIK INC A DELAWARE CORPO RATION"/PA OR "TULARIK INC."/PA OR "TULARIK INCORPORATED"/PA OR "TULARIK LIMITED"/PA OR "TULARIK LTD., LONDON, GB"/PA OR "TULARI K, INC. "/PA OR "TULARIK, INC., SOUTH SAN FRANCISCO, CALIF., US"/PA)

=> s 110 and (OXYSTEROL or OXIDOCHOLESTEROL or EPOXYCHOLESTEROL or t0314407 or t0901317) 19 L10 AND (OXYSTEROL OR OXIDOCHOLESTEROL OR EPOXYCHOLESTEROL OR L11T0314407 OR T0901317)

=> d ibib 1-19

ANSWER 1 OF 19 L11 ACCESSION NUMBER: TITLE (ENGLISH): TITLE (FRENCH): INVENTOR(S):

COPYRIGHT 2005 Univentio on STN PCTFULL 2003063796 PCTFULL ED 20030818 EW 200332 HETEROCYCLIC ARYLSULFONAMIDOBENZYLIC COMPOUNDS COMPOSES ARYLSULFONAMIDOBENZYLIQUES HETEROCYCLIQUES JIAO, Xian, Yun, 1738 South Grant Street, Apt. 5, San Mateo, CA 94402, US [CN, US];

KAYSER, Frank, 4150 17th Street, #25, San Francisco, CA 94114, US [DE, US];

KOPECKY, David, J., 788 Harrison Street, Apt. #507, San

Francisco, CA 94107, US [US, US]; PIPER, Derek, E., 1226 Church Street, #10, San

Francisco, CA 94114, US [US, US];

SHIAU, Andrew, K., 34 Hugo Street, Apt. 3, San

Francsico, CA 94122, US [US, US];

MCKENDRY, Sharon, 950 Redwood Shores Parkway, Apt. A105, Redwood City, CA 94065-8482, US [GB, US]

PATENT ASSIGNEE(S):

TULARIK INC., Two Corporate Drive, South San

Francisco, CA 94080, US [US, US], for all designates

States except US;

JIAO, Xian, Yun, 1738 South Grant Street, Apt. 5, San

Mateo, CA 94402, US [CN, US], for US only;

KAYSER, Frank, 4150 17th Street, #25, San Francisco, CA

94114, US [DE, US], for US only;

KOPECKY, David, J., 788 Harrison Street, Apt. #507, San

Francisco, CA 94107, US [US, US], for US only; PIPER, Derek, E., 1226 Church Street, #10, San Francisco, CA 94114, US [US, US], for US only; SHIAU, Andrew, K., 34 Hugo Street, Apt. 3, San Francsico, CA 94122, US [US, US], for US only; MCKENDRY, Sharon, 950 Redwood Shores Parkway, Apt. A105, Redwood City, CA 94065-8482, US [GB, US], for US

only

KEZER, William, B.\$, Townsend and Townsend and Crew

LLP, Two Embarcadero Center, 8th Floor, San Francisco,

CA 94111\$, US

LANGUAGE OF FILING: LANGUAGE OF PUBL.:

AGENT:

English English Patent

DOCUMENT TYPE: PATENT INFORMATION:

> NUMBER KIND DATE WO 2003063796 A2 20030807

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

RW (ARIPO): RW (EAPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

AM AZ BY KG KZ MD RU TJ TM

RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU

MC NL PT SE SI SK TR

BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG RW (OAPI):

BF BJ CF CG C1 CM GA GN GQ GW HL WO 2003-US3148 A 20030129 2002-60/353,496 20020130

APPLICATION INFO.: PRIORITY INFO.:

20020130

```
L11
      ANSWER 2 OF 19
                        PCTFULL
                                  COPYRIGHT 2005 Univentio on STN
                       2003063576 PCTFULL ED 20030818 EW 200332
ACCESSION NUMBER:
TITLE (ENGLISH):
                       ARYLSULFONAMIDOBENZYLIC COMPOUNDS
TITLE (FRENCH):
                       COMPOSES ARYLSULFONAMIDOBENZYLIQUES
INVENTOR(S):
                       JIAO, Xian, Yun, 1738 South Grant Street, Apt. 5, San
                       Mateo, CA 94402, US [CN, US];
                       KAYSER, Frank, 4150 17th Street, #25, San Francisco, CA
                        94114, US [DE, US];
                       KOPECKY, David, J., 788 Harrison Street, Apt. #507, San
                       Francisco, CA 94107, US [US, US];
                       MCKENDRY, Sharon, 231 30th Street, San Francisco, CA
                       94131, US [GB, US];
                       PIPER, Derek, E., 1226 Church Street, #10, San
                       Francisco, CA 94114, US [US, US];
                       SHIAU, Andrew, K., 34 Hugo Street, Apt. 3, San
                       Francsico, CA 94122, US [US, US]
PATENT ASSIGNEE(S):
                       TULARIK INC., Two Corporate Drive, South San
                       Francisco, CA 94080, US [US, US], for all designates
                       States except US;
                       JIAO, Xian, Yun, 1738 South Grant Street, Apt. 5, San
                       Mateo, CA 94402, US [CN, US], for US only;
                       KAYSER, Frank, 4150 17th Street, #25, San Francisco, CA
                        94114, US [DE, US], for US only;
                       KOPECKY, David, J., 788 Harrison Street, Apt. #507, San
                       Francisco, CA 94107, US [US, US], for US only;
                       MCKENDRY, Sharon, 231 30th Street, San Francisco, CA
                        94131, US [GB, US], for US only;
                        PIPER, Derek, E., 1226 Church Street, #10, San
                       Francisco, CA 94114, US [US, US], for US only;
                       SHIAU, Andrew, K., 34 Hugo Street, Apt. 3, San
                       Francsico, CA 94122, US [US, US], for US only
AGENT:
                       KEZER, William, B.$, Townsend and Townsend and Crew
                       LLP, Two Embarcadero Center, 8th Floor, San Francisco,
                       CA 94111$, US
LANGUAGE OF FILING:
                       English
LANGUAGE OF PUBL.:
                       English
DOCUMENT TYPE:
                       Patent
PATENT INFORMATION:
                       NUMBER
                                         KIND
                                                  DATE
                        ______
                       WO 2003063576
                                           A2 20030807
DESIGNATED STATES
                       AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
      W:
                       CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID
                       IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD
                       MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG
                       SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
      RW (ARIPO):
                       GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
      RW (EAPO):
                       AM AZ BY KG KZ MD RU TJ TM
      RW (EPO):
                       AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU
                       MC NL PT SE SI SK TR
      RW (OAPI):
                       BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
APPLICATION INFO.:
                       WO 2003-US3149 A 20030129
PRIORITY INFO.:
                       2002-60/353,497
                                           20020130
                       US 2002-60/353,497
                                              20020130
L11
      ANSWER 3 OF 19
                        PCTFULL COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER:
                       2001082917 PCTFULL ED 20020826
TITLE (ENGLISH):
                       TREATMENT OF HYPERTRIGLYCERIDEMIA AND OTHER CONDITIONS
                       USING LXR MODULATORS
TITLE (FRENCH):
                       TRAITEMENT DE L'HYPERTRIGLYCERIDEMIE ET D'AUTRES
                       MALADIES AU MOYEN DE MODULATEURS LXR
INVENTOR (S):
                       SHAN, Bei;
                       SCHULTZ, Joshua;
                       TU, Hua
```

PATENT ASSIGNEE(S):

TULARIK INC.;

SHAN, Bei;

SCHULTZ, Joshua;

TU, Hua Patent

DOCUMENT TYPE:

PATENT INFORMATION:

KIND DATE NUMBER ------WO 2001082917 A2 20011108

DESIGNATED STATES

W :

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF

CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:

WO 2001-US14586 A 20010503 2000-60/201,601 20000503

PRIORITY INFO.:

US 2000-60/201,601 20000503

ANSWER 4 OF 19 PCTFULL COPYRIGHT 2005 Univentio on STN

ACCESSION NUMBER: 2001079272 PCTFULL ED 20020826
TITLE (ENGLISH): SITOSTEROLEMIA SUSCEPTIBILITY GENE (SSG): COMPOSITIONS

AND METHODS OF USE

TITLE (FRENCH):

GENE DE SUSCEPTIBILITE A LA SITOSTEROLEMIE (SSG):

COMPOSITIONS ET METHODES D'UTILISATION

INVENTOR(S):

TIAN, Hui;

SCHULTZ, Joshua;

SHAN, Bei

PATENT ASSIGNEE(S):

TULARIK INC.;

TIAN, Hui;

SCHULTZ, Joshua;

SHAN, Bei

Patent

DOCUMENT TYPE:

PATENT INFORMATION:

NUMBER KIND DATE ------

WO 2001079272 A2 20011025

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: PRIORITY INFO.:

WO 2001-US12758 A 20010418 2000-60/198,465 20000418 US 2000-60/204,234 20000515 US 2000-60/204,234 20000515

ANSWER 5 OF 19 L11

PATENT ASSIGNEE(S):

TITLE (ENGLISH):

PCTFULL COPYRIGHT 2005 Univentio on STN

ACCESSION NUMBER: 2001077067 PCTFULL ED 20020822

SOLID PHASE SYNTHESIS OF LXR LIGANDS SYNTHESE EN PHASE SOLIDE POUR LIGANDS LXR

TITLE (FRENCH): INVENTOR(S): MEDINA, Julio;

IMAZAKI, Naonori

TULARIK INC.;

SUMITOMO PHARMACEUTICALS:

MEDINA, Julio; IMAZAKI, Naonori

DOCUMENT TYPE:

Patent

PATENT INFORMATION:

KIND DATE NUMBER -----

WO 2001077067 A2 20011018

DESIGNATED STATES

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU W : CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN

> IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM

> TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY

DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF

CG CI CM GA GN GW ML MR NE SN TD TG

WO 2001-US11242 A 20010405 2000-60/194,911 20000405 APPLICATION INFO.: PRIORITY INFO.:

US 2000-60/194,911 20000405 US 2001-09/827,837

US 2001-09/827,837 20010404 US 2001-09/827,837 20010404

ANSWER 6 OF 19 L11 PCTFULL COPYRIGHT 2005 Univentio on STN

ACCESSION NUMBER: 2001060818 PCTFULL ED 20020822 TITLE (ENGLISH): LXR MODULATORS

TITLE (FRENCH): MODULATEURS LXR LI, Leping; INVENTOR(S):

MEDINA, Julio, Cesar;

SHAN, Bei

PATENT ASSIGNEE(S): TULARIK INC.

DOCUMENT TYPE: Patent

PATENT INFORMATION:

KIND DATE NUMBER ------WO 2001060818 A1 20010823

DESIGNATED STATES

W:

AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML

MR NE SN TD TG

APPLICATION INFO.: WO 2000-US3806 A 20000214

L11 ANSWER 7 OF 19 PCTFULL COPYRIGHT 2005 Univentio on STN ACCESSION NUMBER: 2001051045 PCTFULL ED 20020827 TITLE (ENGLISH): MODULATORS OF THE CONSTITUTIVE ADROSTANE RECEPTOR

(CAR): SCREENING AND TREATMENT OF HYPERCHOLESTEROLEMIA

MODULATEURS DE CAR : CRIBLAGE ET TRAITEMENT DE TITLE (FRENCH):

L'HYPERCHOLESTEROLEMIE INVENTOR (S): LEHMANN, Jurgen, M.;

SHIAU, Andrew, Kwan-Nan

PATENT ASSIGNEE(S): TULARIK INC.;

LEHMANN, Jurgen, M.;

SHIAU, Andrew, Kwan-Nan

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER KIND DATE ------

WO 2001051045 A2 20010719

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF

CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: PRIORITY INFO.:

WO 2001-US1111 A 20010112 2000-60/176,398 20000113 US 2000-60/176,398 20000113

ANSWER 8 OF 19 PCTFULL COPYRIGHT 2005 Univentio on STN ACCESSION NUMBER: 2001003705 PCTFULL ED 20020020
TITLE (ENGLISH): COMPOSITIONS AND METHODS FOR RAISING HDL CHOLESTEROL LEVELS TITLE (FRENCH): COMPOSITIONS ET METHODES PERMETTANT D'AUGMENTER LES TAUX DE HDL CHOLESTEROL INVENTOR(S): SHAN, Bei PATENT ASSIGNEE(S): TULARIK INC.; SHAN, Bei DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER KIND DATE -----WO 2001003705 A1 20010118 DESIGNATED STATES W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG WO 2000-US18533 A 20000707 1999-60/142,994 19990708 APPLICATION INFO.: PRIORITY INFO.: US 1999-60/142,994 19990708 US 2000-09/612,135 20000707 US 2000-09/612,135 20000707 1.11 ANSWER 9 OF 19 PCTFULL COPYRIGHT 2005 Univentio on STN ACCESSION NUMBER: 2000054759 PCTFULL ED 20020515 TITLE (ENGLISH): LXR MODULATORS TITLE (FRENCH): MODULATEURS DU LXR INVENTOR(S): LI, Leping; MEDINA, Julio, C.; HASEGAWA, Hirohiko; CUTLER, Serena, T.; LIU, Jiwen; ZHU, Liusheng; SHAN, Bei; LUSTIG, Kevin PATENT ASSIGNEE(S): TULARIK INC. LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION: KIND DATE NUMBER -----WO 2000054759 A2 20000921 DESIGNATED STATES AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE W: DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG WO 2000-US6611 A 20000315 1999-60/124,525 19990315 US 1999-60/124,525 19990315 APPLICATION INFO.: PRIORITY INFO.: ANSWER 10 OF 19 PCTFULL COPYRIGHT 2005 Univentio on STN ACCESSION NUMBER: 2000040965 PCTFULL ED 20020515 TITLE (ENGLISH): FXR RECEPTOR-MEDIATED MODULATION OF CHOLESTEROL METABOLISM TITLE (FRENCH): MODULATION DU METABOLISME DU CHOLESTEROL INDUITE PAR LE

RECEPTEUR FXR

INVENTOR(S): SHAN, Bei;

OKAMOTO, Arthur, Y.

PATENT ASSIGNEE(S):

TULARIK, INC.

LANGUAGE OF PUBL.: DOCUMENT TYPE:

English

Patent

PATENT INFORMATION:

NUMBER KIND DATE

_____ WO 2000040965

A1 20000713

DESIGNATED STATES

W:

AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML

MR NE SN TD TG

APPLICATION INFO.: PRIORITY INFO.:

WO 2000-US431 A 20000106 1999-60/115,249 19990107 US 1999-60/115,249 19990107

ANSWER 11 OF 19 PCTFULL COPYRIGHT 2005 Univentio on STN

ACCESSION NUMBER: 1999027365 PCTFULL ED 20020515
TITLE (ENGLISH): NUCLEAR HORMONE RECEPTOR DRUG SCREENS

TITLE (FRENCH):

CRIBLES POUR MEDICAMENTS RECEPTEURS DE L'HORMONE

NUCLEAIRE

INVENTOR(S):

LUSTIG, Kevin; BAEUERLE, Patrick; BECKMANN, Holger; CHEN, Jin-Long;

SHAN, Bei PATENT ASSIGNEE(S): TULARIK INC. **TULAKIK** English

LANGUAGE OF PUBL.: DOCUMENT TYPE:

Patent

PATENT INFORMATION:

KIND DATE NUMBER

WO 9927365

DESIGNATED STATES

W:

AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

A1 19990603

APPLICATION INFO.: PRIORITY INFO.:

WO 1998-US24969 A 19981120 1997-08/975,614 19971121 US 1997-08/975,614 19971121 US 1998-09/163,713 19980930 US 1998-09/163,713 19980930

L11 ANSWER 12 OF 19 USPATFULL on STN

TITLE:

ACCESSION NUMBER: 2004:196827 USPATFULL

INVENTOR(S):

Solid phase synthesis of LXR ligands

Medina, Julio, San Carlos, CA, UNITED STATES Imazaki, Naonori, Osaka, JAPAN

PATENT ASSIGNEE(S):

Tularik Inc., So. San Francisco, CA (U.S.

corporation)

Sumitomo Pharmaceuticals Co., Ltd., Osaka, JAPAN (U.S.

corporation)

NUMBER KIND DATE PATENT INFORMATION: US 2004152132 A1 20040805 APPLICATION INFO.: US 2003-749530 A1 20031230 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-827837, filed on 4 Apr

NUMBER DATE -----

US 2000-194911P 20000405 (60) PRIORITY INFORMATION:

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO

CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 3 Drawing Page(s)

LINE COUNT: 1136

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 13 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2003:325111 USPATFULL

TITLE: Arylsulfonamidobenzylic compounds

INVENTOR(S): Jiao, Xian Yun, San Mateo, CA, UNITED STATES

> Kayser, Frank, San Francisco, CA, UNITED STATES McKendry, Sharon, Redwood Shores, CA, UNITED STATES Piper, Derek E., Foster City, CA, UNITED STATES Shiau, Andrew K., San Francisco, CA, UNITED STATES

Tularik Inc., So. San Francisco, CA (U.S. PATENT ASSIGNEE(S):

corporation)

NUMBER KIND DATE -----US 2003229093 A1 20031211 US 2003-354922 A1 20030129 PATENT INFORMATION:

APPLICATION INFO.: A1 20030129 (10)

> NUMBER DATE -----

PRIORITY INFORMATION: US 2002-353497P 20020130 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO

CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834

NUMBER OF CLAIMS: 36 EXEMPLARY CLAIM: LINE COUNT: 3129

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 14 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2003:312734 USPATFULL

TITLE: Heterocyclic arylsulfonamidobenzylic compounds INVENTOR(S):

Jiao, Xian Yun, San Mateo, CA, UNITED STATES Kayser, Frank, San Francisco, CA, UNITED STATES Kopecky, David J., San Francisco, CA, UNITED STATES McKendry, Sharon, Redwood Shores, CA, UNITED STATES Piper, Derek E., Foster City, CA, UNITED STATES

Shiau, Andrew K., San Francisco, CA, UNITED STATES

PATENT ASSIGNEE(S): Tularik Inc., So. San Francisco, CA (U.S.

corporation)

NUMBER KIND DATE -----PATENT INFORMATION: US 2003220339 A1 20031127 US 2003-354923 A1 20030129 APPLICATION INFO.: (10)

NUMBER DATE

PRIORITY INFORMATION: US 2002-353496P 20020130 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO

CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834

NUMBER OF CLAIMS:

EXEMPLARY CLAIM: LINE COUNT: 1971

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 15 OF 19 USPATFULL on STN

2003:115720 USPATFULL ACCESSION NUMBER:

TITLE: Nuclear hormone receptor fluorescence polarization

assay

INVENTOR(S): Lustig, Kevin, South San Francisco, CA, United States

Baeuerle, Patrick, South San Francisco, CA, United

Beckmann, Holger, South San Francisco, CA, United

States

Chen, Jin-Long, South San Francisco, CA, United States

Shan, Bei, South San Francisco, CA, United States

PATENT ASSIGNEE(S): Tularik Inc., South San Francisco, CA, United

States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6555326	B1	20030429
APPLICATION INFO.:	US 1997-975614		19971121

DOCUMENT TYPE: Utility FILE SEGMENT: GRANTED PRIMARY EXAMINER: Pak, Michael

LEGAL REPRESENTATIVE: Osman, Richard Aton

NUMBER OF CLAIMS: 18 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)

LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 16 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2003:3485 USPATFULL

TITLE: FXR receptor-mediated modulation of cholesterol

metabolism

INVENTOR(S): Shan, Bei, Redwood City, CA, UNITED STATES

Okamoto, Arthur Y., San Mateo, CA, UNITED STATES

PATENT ASSIGNEE(S): Tularik Inc., a Delaware Corporation (U.S.

corporation)

	NUMBER	KIND	DATE	_	
PATENT INFORMATION: APPLICATION INFO.:	US 2003003520 US 2002-217293		20030102 20020812	(10)	

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-47 \$948, filed on 6 Jan

2000, GRANTED, Pat. No. US 6465258

NUMBER DATE -----

PRIORITY INFORMATION: US 1999-115249P 19990107 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO

CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834

NUMBER OF CLAIMS: 47

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 14 Drawing Page(s)

LINE COUNT: 1817

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 17 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2002:268615 USPATFULL

TITLE:

FXR receptor-mediated modulation cholesterol metabolism INVENTOR (S): Shan, Bei, Redwood City, CA, United States

Okamoto, Arthur Y, San Mateo, CA, United States

PATENT ASSIGNEE(S): Tularik, Inc., South San Francisco, CA,

United States (U.S. corporation)

KIND DATE NUMBER ______ US 6465258 B1 PATENT INFORMATION: 20021015 US 2000-478948 20000106 (9) APPLICATION INFO.: NUMBER DATE -----PRIORITY INFORMATION: US 1999-115249P 19990107 (60) Utility DOCUMENT TYPE: GRANTED FILE SEGMENT: PRIMARY EXAMINER: Whisenant, Ethan C. LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP NUMBER OF CLAIMS: 47 EXEMPLARY CLAIM: NUMBER OF DRAWINGS: 14 Drawing Figure(s); 14 Drawing Page(s) LINE COUNT: CAS INDEXING IS AVAILABLE FOR THIS PATENT. L11 ANSWER 18 OF 19 USPATFULL on STN ACCESSION NUMBER: 2001:202683 USPATFULL TITLE: LXR modulators INVENTOR(S): Li, Leping, Burlingame, CA, United States Medina, Julio C., San Carlos, CA, United States Lustig, Kevin, South San Francisco, CA, United States Shan, Bei, Redwood City, CA, United States Hasegawa, Hirohiko, Osaka, Japan Cutler, Serena T., Palo Alto, CA, United States Liu, Jiwen, Burlingame, CA, United States Zhu, Liusheng, Burlingame, CA, United States PATENT ASSIGNEE(S): Tularik Inc., So. San Francisco, CA, United States (U.S. corporation) KIND DATE NUMBER -----US 6316503 B1 20011113 PATENT INFORMATION: 20000314 (9) APPLICATION INFO.: US 2000-525861 DOCUMENT TYPE: Utility FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Lambkin, Deborah C. LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP NUMBER OF CLAIMS: 47 EXEMPLARY CLAIM: NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s) LINE COUNT: 2631 CAS INDEXING IS AVAILABLE FOR THIS PATENT. L11 ANSWER 19 OF 19 USPAT2 on STN 2002:141091 USPAT2 ACCESSION NUMBER: TITLE: Solid phase synthesis of LXR ligands INVENTOR(S): Medina, Julio, San Carlos, CA, United States Imazaki, Naonori, Osaka, JAPAN PATENT ASSIGNEE(S): Tularik, Inc., So. San Francisco, CA, United States (U.S. corporation) Sumitomo Pharmaceuticals Co., Ltd., Osaka, JAPAN (non-U.S. corporation) NUMBER KIND DATE PATENT INFORMATION: APPLICATION INFO.: US

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;	6673543	B2	20040106		
;	2001-827837		20010404	(9)	
	NUMBER	DAT	re		
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PRIORITY INFORMATION: US 2000-194911P

20000405 (60)

DOCUMENT TYPE: FILE SEGMENT: PRIMARY EXAMINER:

Utility GRANTED

Celsa, Bennett

ASSISTANT EXAMINER: Epperson, Jon D.

LEGAL REPRESENTATIVE: Townsend and Townsend and Crew LLP

NUMBER OF CLAIMS: 7 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)

LINE COUNT: 1009

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L1

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(FILE 'HOME' ENTERED AT 14:20:43 ON 09 MAY 2005)

FILE 'CAPLUS' ENTERED AT 14:20:48 ON 09 MAY 2005

1 S WO9910320/PN

L2 0 S L1 AND (OXYSTEROL OR (EPOXYCHOLESTEROL) OR OXIDOCHOLESTEROL)

FILE 'REGISTRY' ENTERED AT 14:32:53 ON 09 MAY 2005

E T0314407/CN

E T 314407/CN

E T 0314407/CN

L3 1 S E3

FILE 'CAPLUS' ENTERED AT 14:33:54 ON 09 MAY 2005

4 S L3 OR T(W) 0314407 OR T0314407

FILE 'REGISTRY' ENTERED AT 14:36:12 ON 09 MAY 2005

E T 0901317/CN

L5 1 S E3

FILE 'CAPLUS' ENTERED AT 14:36:54 ON 09 MAY 2005

85 S L5 OR T(W)0901317 OR T0901317

17 S L6(L) (HYPERCHOLESTER? OR HYPERLIP? OR ATHEROSCLERO? OR DIABET

4 S L6 NOT PY>=2002

$$F_3C-CH_2-N$$

$$Ph-S=0$$

$$0$$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN Benzenesulfonamide, N-(2,2,2-trifluoroethyl)-N-[4-[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:

CN T 0901317 CN TO 901317 n str cn

ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN 293753-06-7 REGISTRY

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN Benzenesulfonamide, N-methyl-N-[4-[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:

CN T 0314407

ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN ACCESSION NUMBER: 2002:574920 CAPLUS DOCUMENT NUMBER: 137:140337 TITLE: Preparation of hydroxyhexafluoropropylarenes as malonyl-CoA decarboxylase inhibitors. Arrhenius, Thomas; Chen, Mi; Cheng, Jie Fei; Haramura, INVENTOR(S): Masayuki; Huang, Yujin; Nadzan, Alex; Tith, Sovouthy; Wallace, David; Zhang, Lin; Brown, Steve; Harmon, Charles PATENT ASSIGNEE(S): Chugai Seiyaku Kabushiki Kaisha, Japan SOURCE: PCT Int. Appl., 63 pp. CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. ------____ WO 2002-US1814 WO 2002058690 A2 20020801 20020122 A3 WO 2002058690 20030424 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG EP 1353662 A2 20031022 EP 2002-703196 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR JP 2004521113 T2 20040715 JP 2002-559024 20020122 US 2004087627 A1 20040506 US 2003-466856 20030721 PRIORITY APPLN. INFO.: US 2001-264552P P 20010126. P 20010126 US 2001-265380P WO 2002-US1814 W 20020122 OTHER SOURCE(S): CASREACT 137:140337; MARPAT 137:140337 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN ACCESSION NUMBER: 2001:816445 CAPLUS DOCUMENT NUMBER: 135:352751 TITLE: Treatment of hypertriglyceridemia and other conditions using nuclear receptor LXR modulators INVENTOR(S): Shan, Bei; Schultz, Joshua; Tu, Hua PATENT ASSIGNEE(S): Tularik Inc., USA PCT Int. Appl., 60 pp. SOURCE: CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE -------------------WO 2001082917 A2 20011108 WO 2001-US14586 20010503 WO 2001082917 **A**3 20020606 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,

BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002048572 A1 20020425 US 2001-848990 20010503 PRIORITY APPLN. INFO.: US 2000-201601P P 20000503

ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:863226 CAPLUS

DOCUMENT NUMBER: 135:41708

TITLE: Role of LXRs in control of lipogenesis

AUTHOR(S): Schultz, Joshua R.; Tu, Hua; Luk, Alvin; Repa, Joyce J.; Medina, Julio C.; Li, Leping; Schwendner, Susan;

Wang, Shelley; Thoolen, Martin; Mangelsdorf, David J.;

Lustig, Kevin D.; Shan, Bei

CORPORATE SOURCE: Tularik Inc., South San Francisco, CA, 94080, USA

SOURCE: Genes & Development (2000), 14(22), 2831-2838

CODEN: GEDEEP; ISSN: 0890-9369

PUBLISHER: Cold Spring Harbor Laboratory Press

DOCUMENT TYPE: Journal LANGUAGE: English

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:666587 CAPLUS

DOCUMENT NUMBER: 133:237693

TITLE: Preparation of bis(trifluoromethyl)hydroxymethylbenzen

esulfonamides, -ureas, and -carbamates as liver X

receptor modulators.

INVENTOR(S): Li, Leping; Medina, Julio C.; Hasegawa, Hirohiko;

Cutler, Serena T.; Liu, Jiwen; Zhu, Liusheng; Shan,

Bei; Lustig, Kevin Tularik Inc., USA

SOURCE: PCT Int. Appl., 113 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT ASSIGNEE(S):

		PATENT NO.									APPLICATION NO.								
	WO	2000054759 2000054759			A2 20000921			WO 2000-US6611											
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		W :						ΑZ,											
			CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	
			ΙL,	IN,	IS,	JP,	KE,	KG,	KΡ;	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	
			MA,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	
								TR,											
								RU,											
		RW:	GH,	GM,	ΚE,	LS,	MW,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	BE,	CH,	CY,	DE,	
								GR,											
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								EP 2000-914958											
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ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:642687 CAPLUS

135:366556 DOCUMENT NUMBER:

Hypolipidemic effects of selective liver X receptor TITLE:

alpha agonists

AUTHOR (S): Song, Ching; Liao, Shutsung

CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, the

> Tang Center for Herbal Medicine Research, The Ben May Institute for Cancer Research, Chicago, IL, 60637, USA

Steroids (2001), 66(9), 673-681 SOURCE:

CODEN: STEDAM; ISSN: 0039-128X

PUBLISHER: Elsevier Science Inc.

Journal DOCUMENT TYPE: LANGUAGE: English

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:202081 CAPLUS

TITLE: Discovery and optimization of activators of the

nuclear receptor LXR

AUTHOR(S): Medina, Julio C.; Li, Leping; Cutler, Serena;

Hasegawa, Hirohiko; Liu, Jiwen; Zhu, Liusheng;

Schultz, Joshua R.; Shan, Bei

CORPORATE SOURCE: Department of Chemistry, Tularik Inc, South San

Francisco, CA, 94080, USA

Abstracts of Papers, 221st ACS National Meeting, San. SOURCE:

Diego, CA, United States, April 1-5, 2001 (2001)

MEDI-180

CODEN: 69FZD4

American Chemical Society PUBLISHER: DOCUMENT TYPE: Journal; Meeting Abstract

LANGUAGE: English

ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN L8

ACCESSION NUMBER: 2001:141061 CAPLUS

DOCUMENT NUMBER: 134:293193

TITLE: Expression of sterol regulatory element-binding

protein 1c (SREBP-1c) mRNA in rat hepatoma cells

requires endogenous LXR ligands

AUTHOR (S): DeBose-Boyd, Russell A.; Ou, Jiafu; Goldstein, Joseph

L.; Brown, Michael S.

CORPORATE SOURCE: Department of Molecular Genetics, University of Texas

Southwestern Medical Center, Dallas, TX, 75390-9046,

USA

SOURCE: Proceedings of the National Academy of Sciences of the

United States of America (2001), 98(4), 1477-1482

CODEN: PNASA6; ISSN: 0027-8424 National Academy of Sciences

DOCUMENT TYPE: Journal

PUBLISHER:

LANGUAGE: English

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN L8

ACCESSION NUMBER: 2000:863226 CAPLUS

DOCUMENT NUMBER: 135:41708

TITLE: Role of LXRs in control of lipogenesis

AUTHOR (S): Schultz, Joshua R.; Tu, Hua; Luk, Alvin; Repa, Joyce

J.; Medina, Julio C.; Li, Leping; Schwendner, Susan; Wang, Shelley; Thoolen, Martin; Mangelsdorf, David J.;

Lustig, Kevin D.; Shan, Bei

CORPORATE SOURCE: Tularik Inc., South San Francisco, CA, 94080, USA

SOURCE: Genes & Development (2000), 14(22), 2831-2838

CODEN: GEDEEP; ISSN: 0890-9369

PUBLISHER: Cold Spring Harbor Laboratory Press ANSWER 8 OF 1116 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:277969 CAPLUS

TITLE: Oxidation of steroidal alkenes: Syntheses of

oxysterols

AUTHOR (S): Qiu, Zhihai

CORPORATE SOURCE: Auburn Univ., Auburn, AL, USA

SOURCE: (2004) 130 pp. Avail.: UMI, Order No. DA3124290

From: Diss. Abstr. Int., B 2004, 65(2), 746

DOCUMENT TYPE: Dissertation

LANGUAGE: English

Oxidation of steroidal alkenes: Syntheses of oxysterols

ANSWER 9 OF 1116 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:272371 CAPLUS

TITLE:

Novel Routes for Metabolism of 7-Ketocholesterol

AUTHOR (S): Jessup, Wendy; Brown, Andrew J.

CORPORATE SOURCE: Centre for Vascular Research at School of Medical

Sciences, University of New South Wales, Sydney, Australia and Department of Haematology, Prince of

Wales Hospital, Sydney, Australia

SOURCE: Rejuvenation Research (2005), 8(1), 9-12

CODEN: RREEC2; ISSN: 1549-1684

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal LANGUAGE: English

Oxysterols (oxygenated forms of cholesterol) are present at low levels in the circulation and accumulate is plasma and tissues in some pathologies. In atherosclerotic lesions, 7-oxygenated oxysterols , predominantly 7-ketocholesterol, accumulate and have been implicated in the pathol. of the disease. Therefore, knowledge of the mechanisms for 7-ketocholesterol generation and metabolism may provide therapeutic drug targets. There is some in vivo and in vitro evidence that sterol 27-hydroxylase acts on 7-ketocholesterol to initiate its degradation to more polar, water-soluble products. Recent studies indicate an alternative mechanism, in which 7-ketocholesterol is reduced to 7β hydroxycholesterol by 11β -hydroxysteroid dehydrogenase type 1.

L6 ANSWER 41 OF 55 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:127600 CAPLUS

DOCUMENT NUMBER: 124:199411

TITLE: Oxysterols present in atherosclerotic tissue decrease

the expression of lipoprotein lipase messenger RNA in

human monocyte-derived macrophages

AUTHOR(S): Hulten, Lilemor Mattsson; Lindmark, Helena;

Diczfalusy, Ulf; Bjoerkhem, Ingemar; Ottosson, Malin;

Liu, Yani; Bondjers, Goeran; Wiklund, Olov

CORPORATE SOURCE: Wallenbergy Laboratory for Cardiovascular Research,

University of Goeteborg, Goeteborg, S-413 45, Swed. Journal of Clinical Investigation (1996), 97(2), 461-8

CODEN: JCINAO; ISSN: 0021-9738

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal LANGUAGE: English

SOURCE:

The presence of oxysterols in macrophages isolated from atherosclerotic tissue and the effect of oxysterols on the regulation of lipoprotein lipase (LPL) mRNA were studied. Both rabbit and human macrophages, freshly isolated from atherosclerotic aorta, show about the same distribution of oxysterols, analyzed by isotope dilution mass spectrometry, except that all three prepns. of human arterial-derived macrophages contained high levels of 27-hydroxycholesterol, which was not found in rabbit macrophages. To determine if oxysterols regulate LPL expression, human monocyte-derived macrophages were incubated with different oxysterols. Incubation with 7β -hydroxycholesterol and 25-hydroxycholesterol resulted in a 70-75% reduction of LPL mRNA, analyzed by quant. RT-PCR. Cholesterol and other tested oxysterols showed no effect on macrophage LPL mRNA expression compared with control. LPL activity in the medium was also reduced after exposure of the macrophages to 7β hydroxycholesterol and 25-hydroxycholesterol. In conclusion, the authors have demonstrated accumulation of oxysterols in macrophage-derived foam cells isolated from atherosclerotic aorta. There was suppression of LPL mRNA in human monocyte-derived macrophages after incubation with 7β -hydroxycholesterol and 25-hydroxycholesterol. It is tempting to suggest that an exposure to oxysterols may explain the earlier observation of a low level of LPL mRNA in arterial foam cells. ΤТ

57-88-5, Cholesterol, biological studies 566-26-7, 7α-Hydroxycholesterol 566-28-9, 7-Ketocholesterol 1250-95-9,

 5α , 6α - Epoxycholesterol 1253-84-5,

Cholestane- 3β , 5α , 6β -triol 4025-59-6, 5β , 6β -

Epoxycholesterol 30271-38-6, 24-Hydroxycholesterol

RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(oxysterol accumulation in rabbit and human macrophage-derived foam cells and effect of oxysterols on lipoprotein lipase mRNA expression in human monocyte-derived macrophages)

ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1994:548787 CAPLUS

DOCUMENT NUMBER: 121:148787

TITLE: Effects of a 2,3-oxidosqualene-lanosterol cyclase

> inhibitor, 2,3: 22,23-dioxidosqualene and 24,25-epoxycholesterol on the regulation of

cholesterol biosynthesis in human hepatoma cell line

HepG2

AUTHOR(S): Dollis, Daniele; Schuber, Francis

CORPORATE SOURCE: Laboratoire Chimie Bioorganique, Faculte Pharmacie,

Illkirch, 67400, Fr.

SOURCE: Biochemical Pharmacology (1994), 48(1), 49-57

CODEN: BCPCA6; ISSN: 0006-2952

DOCUMENT TYPE: Journal

LANGUAGE: English

24,25-Epoxycholesterol

RL: BIOL (Biological stu

N-[1(1,5,9)-trimethyldecyl]-4 α , 10-dimethyl-8-aza-trans-decal-3 β -ol (8-azadecalin 1), a high-energy intermediate analog for the 2,3-oxidosqualene-lanosterol cyclase, was found to be a powerful (IC50 \approx 0.1 μ M) inhibitor of cholesterol biosynthesis in human hepatoma HepG2 cells. In anal. with other mammalian cells grown in the presence of cyclase inhibitors, the decrease in C27-sterol formation was accompanied by an accumulation of 2,3-oxidosqualene, 2,3:22,23dioxidosqualene, and by the formation of a compound characterized as 24,25-epoxycholesterol, a repressor of HMG-CoA (3-hydroxy-3-methylglutaryl COA) reductase activity. In order to assess the cyclase as a potential pharmacol. target for the design of hypocholesterolemic drugs, it is important to test whether inhibitors of this enzyme are able to act synergistically on the biosynthesis of cholesterol, i.e. by decreasing the amount of lanosterol formed and by repressing the regulatory HMG-COA reductase via the formation of regulatory oxysterols. The accumulation of 24,25-epoxycholesterol in relationship to the decrease of C27-sterol biosynthesis and of HMG-CoA reductase activity showed only a partial correlation: e.g. at [1] = 100 + IC50 only a 50% reduction in enzyme activity could be attained. In contrast, when HepG2 cells were treated with 2,3:22,23-dioxidosqualene or 24,25-epoxycholesterol, excellent correlations were found between the inhibition of C27-sterol biosynthesis and the repression of HMG-CoA reductase activity, which was almost complete at the highest concns. of these epoxides (10-5 M). Altogether, the authors' results suggest that treatment of HepG2 cells with a cyclase inhibitor such as 8-azadecalin (1) does not lead to an intracellular accumulation of repressor mols. high enough to fully trigger a regulatory pathway resulting in a complete down-regulation of HMG-COA reductase. At intermediary concns. of cyclase inhibitors (IC50), however, a synergistic mode of action of these inhibitors seems plausible. TΥ 31063-19-1, 2,3:22,23-Dioxidosqualene 72542-49-5,

104905-12-6

L3 ANSWER 10 OF 1116 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:255894 CAPLUS

TITLE: Epoxidation and reduction of cholesterol,

1,4,6-cholestatrien-3-one and 4,6-cholestadien-3 β -

ol

AUTHOR(S): Ma, Eunsook; Kim, Haksoon; Kim, Eunjeong

CORPORATE SOURCE: College of Pharmacy, Catholic University of Daegu, 330

Geumrak 1-ri, Hayang-eup, Gyongsan-si Gyongbook,

712-702, S. Korea

Steroids (2005), 70(4), 245-250

CODEN: STEDAM; ISSN: 0039-128X

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal LANGUAGE: English

Many naturally occurring polyhydroxylated sterols and oxysterols exhibit potent biol. activities. This paper describes reagent and position selectivity of epoxidn. and reduction of cholesterol derivs. Cholesterol was reacted with m-chloroperoxybenzoic acid (m-CPBA) to form 5α , 6α -epoxycholestan- 3β -ol, but in reaction with 30% H2O2, it did not reacted. 1,4,6-Cholestatrien-3-one was obtained from cholesterol and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in dioxane. 1,4,6-Cholestatrien-3-one was reacted with 30% H2O2 and 5% NaOH in methanol to give $1\alpha, 2\alpha$ -epoxy-4,6-cholestadien-3-one, which was stereoselectively reduced with NaBH4 to form $1\alpha, 2\alpha$ -epoxy-4,6cholestadien- 3β -ol and reduced with Li metal in absolute ethanol to give 2-ethoxy-1,4,6-cholestatrien-3-one. And 1,4,6-cholestatrien-3-one was epoxidized with m-CPBA in dichloromethane to afford $6\alpha,7\alpha$ epoxy-1,4-cholestadien-3-one, which was reacted with NaBH4 to synthesize 6α -hydroxy-4-cholesten-3-one and reduced Li metal in absolute ethanol to form 2-ethoxy-1,4,6-cholestatrien-3-one, resp. 1,4,6-Cholestatrien-3-one was reduced with NaBH4 in absolute ethanol to form 4,6-cholestadien-3βol, which was reacted with 30% H2O2 to leave original compound, but was reacted with m-CPBA to give 4β , 5β -epoxy-6-cholesten-3 β -ol as the major product and 4β , 5β -epoxy- 6α , 7α epoxycholestan- 3β -ol as the minor product.

=> d his

SOURCE:

(FILE 'HOME' ENTERED AT 10:59:49 ON 09 MAY 2005)

FILE 'REGISTRY' ENTERED AT 11:13:41 ON 09 MAY 2005

L1 1 S 72542-49-5

E OXYSTEROL/CN

E OXYSTEROL

L2 193 S E3

FILE 'CAPLUS' ENTERED AT 11:18:14 ON 09 MAY 2005

L3 1116 S OXYSTEROL

L14 ANSWER 5 OF 46 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:38935 CAPLUS

DOCUMENT NUMBER: 130:206522

TITLE: Structural requirements of ligands for the oxysterol

liver X receptors LXR α and LXR β

AUTHOR(S): Janowski, Bethany A.; Grogan, Michael J.; Jones,

Stacey A.; Wisely, G. Bruce; Kliewer, Steven A.;

Corey, Elias J.; Mangelsdorf, David J.

CORPORATE SOURCE: Howard Hughes Medical Institute and Department of

Pharmacology, University of Texas Southwestern Medical

Center at Dallas, Dallas, TX, 75235-9050, USA

Proceedings of the National Academy of Sciences of the

United States of America (1999), 96(1), 266-271

CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal LANGUAGE: English

SOURCE:

LXR α and $-\beta$ are nuclear receptors that regulate the metabolism of several important lipids, including cholesterol and bile acids. Previously, we have proposed that LXRs regulate these pathways through their interaction with specific, naturally occurring oxysterols, including 22(R)-hydroxycholesterol, 24(S)-hydroxycholesterol, and 24(S), 25-epoxycholesterol. Using a ligand binding assay that incorporates scintillation proximity technol. to circumvent many of the problems associated with assaying extremely hydrophobic ligands, we now demonstrate that these oxysterols bind directly to LXRs at concns. that occur in vivo. To characterize further the structural determinants required for potent LXR ligands, we synthesized and tested a series of related compds. for binding to LXRs and activation of transcription. These studies revealed that position-specific monoxidn. of the sterol side chain is requisite for LXR high-affinity binding and activation. Enhanced binding and activation can also be achieved through the use of 24-oxo ligands that act as hydrogen bond acceptors in the side chain. In addition, introduction of an oxygen on the sterol B-ring results in a ligand with $LXR\alpha$ -subtype selectivity. These results support the hypothesis that naturally occurring oxysterols are physiol. ligands for LXRs and show that a rational, structure-based approach can be used to design potent LXR ligands for pharmacol. use.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

69/848,990

L9 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1985:557930 CAPLUS

DOCUMENT NUMBER:

103:157930

TITLE:

Identification of regulatory oxysterols,

24(S), 25-epoxycholesterol

and 25-hydroxycholesterol, in cultured

fibroblasts

AUTHOR (S):

SOURCE:

Saucier, Sandra E.; Kandutsch, Andrew A.; Taylor,

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(S), 25-epoxycholesterol and 25

-hydroxycholesterol. The identities of the 2 sterols were established by cochromatog. with authentic samples and by isotopic dilution and recrystn. Only low levels of repressor activity were found in other fractions of sterol extract The endogenous concns. of 24(S),25-epoxycholesterol (7.2 fg/cell) and 25-hydroxycholesterol (1.5

fg/cell) appear to be within the ranges required for the regulation of 3-hydroxy-3-methylglutaryl-CoA reductase.

TI Identification of regulatory oxysterols, 24(S),
25-epoxycholesterol and 25-hydroxycholesterol,
in cultured fibroblasts

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